Status of the claims

Claim 47 has been amended to add the term "the complement of". This amendment adds no new matter.

Claim 52 has been amended to substitute the term "nucleic acid disclosed in" for the term "a nucleic acid sequence of", as suggested by the Examiner. This amendment adds no new matter.

Claims 47 and 52 have been amended to delete the term "when the monomer is in a functional tetrameric form". This amendment adds no new matter.

Rejections under 35 U.S.C. § 112, second paragraph

Molecular weight

Claims 45, 50 and 55 are rejected as allegedly indefinite for reciting molecular weight values. In order to expedite prosecution, claim 45 has been canceled. With respect to claims 50 and 55, Applicants respectfully traverse the rejection. On page 10, lines 23-25, Applicants disclose the molecular weight of mSlo3 and hSlo3 to be 126 kDa. Methods of measuring molecular weight are well known in the art. One of skill would understand how to determine the molecular weight of hSlo3 by using standard methods such as SDS-PAGE or chromatography using standard molecular weight markers. Furthermore, Applicants reference standard molecular biology texts such as Sambrook and Ausubel, which describe such methodologies (*see e.g.,* specification page 29, lines 3-6). The Examiner alleges that a value for molecular weight is dependent upon the method by which it is determined and differs with different methods. Nevertheless, one of skill in the art would know how to find the method which produces a molecular weight of 126 kDa for hSlo3. The specification and claims therefore meet the threshold clarity and precision standards of the statute. MPEP § 2173.02. As described by the court in *In re Chilowsky*:

> It is well settled that the disclosure of an application embraces not only what is expressly set forth in words or drawings, but what would be

> understood by persons skilled in the art. . . . That which is common and well known is as if it were written out in the patent. *In re Chilowsky*, 108 USPQ 321, 324 (C.C.P.A. 1956)

Applicants therefore respectfully request that the rejection be withdrawn.

Sequences as mere characters on a page

Claim 17 is rejected as allegedly indefinite for claiming antibodies generated against SEQ ID NOs that are mere characters on a page. In order to expedite prosecution, claim 17 has been canceled without prejudice to subsequent revival.

Claim 52 is rejected as allegedly indefinite for referring to nucleic acids that hybridize to a nucleic acid sequence of certain SEQ ID NOs because the sequences are mere characters on a page. In response, as suggested by the Examiner, Applicants have amended the claim to recite nucleic acids that hybridize to the nucleic acids disclosed in the SEQ ID NOs. Applicants therefore respectfully request that the rejection be withdrawn.

Specifically binding

Claim 17 is rejected as allegedly indefinite for reciting the term "specifically binding". In order to expedite prosecution, claim 17 has been canceled.

Unit conductance

Claims 17, 47 and 52 are rejected as allegedly indefinite for reciting the term "unit conductance". In order to expedite prosecution, claim 17 has been canceled. With respect to claims 47 and 52, Applicants respectfully traverse. The Examiner alleges that the conditions under which unit conductance is determined are not disclosed and that without the disclosure of said conditions, it cannot be dictated which polypeptides are encompassed by the claim. Under the definition section of the specification, page 13 line 31 to page 14, line 3, Applicants disclose that the unitary conductance is measured under a symmetrical potassium concentration of 160mM in a *Xenopus* oocyte using the

conditions specified in Example IV. Example IV on pages 60-61 of the specification specifies the conditions. For whole cell-recording, medium nd96 supplemented with 1mM DIDS was employed as a bath solution. Patches were perfused with either 0 CA2+ EGTA solutions or Ca2+ containing 184 K gluconate, 10 KOH, 10 HEPES, 200 mM hemicalcium gluconate solutions. The pipet solution contained 0.5 K gluconate, 0.5 kCI, 1.1 KOH, 10 HEPES, 159 Na gluconate and 2 hemiMg gluconate, pH 7.1. Applicants assert that one of skill in the art, using these disclosed conditions, would know how to measure the unit conductance of the claimed proteins. The specification and claims therefore meet the clarity and precision standards of the statute. Furthermore, the term unit conductance is a term of art that a skilled practitioner would understand. Applicants therefore respectfully request that the rejection be withdrawn.

Approximately

The Examiner objects to claims 17, 46, and 52 because it is allegedly unclear what the term approximately encompasses. In response, Applicants have deleted the word approximately from the claims. Applicants therefore respectfully request that the rejection be withdrawn.

Increased Activity

Claims 17, 47 and 52 are rejected as allegedly indefinite for not defining what activity is increased. In order to expedite prosecution, claim 17 has been canceled. With respect to claims 47 and 52, Applicants respectfully traverse. In the specification, Applicant's use the terms "activity" and "current amplitude" interchangeably. Claims 47 and 52 refer to a potassium channel having increased activity above a certain intracellular pH level of 7.1. On page 14, lines 28-29, it is explained that "pH channels show increased current amplitude above approximately pHi 7.1." On the next line, Applicants disclose that "mSlo3 at a pHi of 6.8 did not show increased activity, while activity was substantially increased at pHi 7.8". Therefore, one of skill in the art would understand

that activity refers to current amplitude when describing potassium channels. Applicants therefore respectfully request that the rejection be withdrawn.

Functional tetrameric form

Claims 17, 47 and 52 are rejected as allegedly indefinite for reciting the term "functional tetrameric form." In response, in order to expedite prosecution, Applicants have deleted the term "functional tetrameric form".

"mSlo3" or "hSlo3"

Claims 19, 48 and 53 are rejected as allegedly indefinite for reciting the terms human or mouse Slo3. In order to expedite prosecution, these claims have been canceled without prejudice to subsequent revival. Accordingly, Applicants respectfully request that the rejection be withdrawn.

Rejection under 35 U.S.C. § 101

Claims 47-56 stand rejected for lacking utility because the claimed invention allegedly lacks a "substantial" or "real world" utility (Office Action, page 7). The Examiner asserts that the Applicants have not disclosed a function associated with the polypeptides of the instant invention or the polynucleotides that encode them or any disease states directly related to their dysfunction. The Examiner also asserts that the specification does not disclose any instances where disorders can be effected by interfering with the activity of the claimed polypeptides. The Examiner alleges that the corresponding utilities of the claimed polypeptides are limited to identifying other nucleic acids that hybridize to said polynucleotides, identifying disease states associated with polypeptide dysfunction or targeting drugs for discovery. According to the Examiner, these asserted utilities are the only utilities known for the claimed polypeptides and are not sufficient as required by the United States Patent Laws. Applicants respectfully traverse. With this amendment, Applicants attach an expert declaration under 37 C.F.R. § 1.132 by Dr. Timothy Jegla explaining that, at the time of the invention, one of skill in

the art would easily recognize a "substantial" or "real world" utility for the claimed polypeptides. In fact, one of skill in the art, after reading the specification, would believe that the claimed polypeptides play a significant role in sperm capacitation.

A. Introduction

According to the MPEP, in order to assess utility, the Examiner should review the specification to determine if there are any statements asserting that the claimed invention is useful for any particular purpose. An invention has utility if the utility is specific, substantial and credible. A utility is specific if it is specific to the subject matter claimed. A utility is substantial if it has a real-world use. In most cases, an applicant's assertion of utility creates a presumption of utility that is sufficient to satisfy the utility requirement of 35 U.S.C. § 101. Furthermore, an Examiner cannot simply dismiss an assertion of a particular utility as wrong but must determine if the assertion is credible, i.e., would be believable to a person of ordinary skill in the art based on the totality of the evidence. (See MPEP 2107.02).

A *prima facie* showing of lack of utility must establish that it is more likely than not that a person of ordinary skill in the art would not consider that any utility asserted by the applicant would be specific and substantial. The present application claims isolated polypeptide monomers of a Slo3 potassium channel expressed in spermatocytes that is activated by changes in intracellular pH and membrane potential. At the time the application was filed, one of skill in the art would recognize the utility of Slo3 potassium channels expressed in spermatocytes. In order to demonstrate that one of skill in the art would recognize the utility of the present invention and appreciate its real world context, Applicants have included a declaration by Dr. Timothy Jegla, Chief Scientist at ICAgen, Inc.

B. Declaration of Dr. Timothy Jegla

In his declaration, Dr. Jegla explains why one of skill in the art would recognize the utility of the present invention. Dr. Jegla's resume is attached hereto as

Exhibit C. According to Dr. Jegla, it is well known in the art that intracellular pH has a profound effect on the viability of mammalian sperm. Applicants submit Exhibits A and B, two references that disclose that alkaline pH is necessary for sperm capacitation and the acrosome reaction. Sperm capacitation is known to be accompanied by increases in potassium permeability that hyperpolarizes the membrane. According to Dr. Jegla, because the newly identified Slo3 is highly and specifically expressed in sperm and is activated by alkalinization, persons of skill in the art would expect that the Slo3 channel plays an important role in sperm capacitation, e.g., by increasing potassium permeability. In fact, according to Dr. Jegla, after reading the present application, persons of skill in the art would expect that Slo3 is an excellent target for candidate compounds that modulate sperm function. Assays for such compounds, using Slo3 as a target, are useful for identifying compounds that affect fertility. For example, persons of skill in the art would expect that Slo3 openers could be used to initiate the capacitation cascade. A Slo3 opener, therefore, could be used to treat certain types of infertility caused by reduced sperm function. Persons of skill in the art would also expect that Slo3 blockers could inhibit or block capacitation and the acrosome reaction. A person of skill in the art would expect that a Slo3 blocker, for example, could be useful as a contraceptive device.

C. The polypeptide monomers of this invention have specific, substantial and credible utility

As noted by the Examiner in the present Office Action, Applicants have shown that the claimed polypeptide monomers form a pH sensitive potassium channel having a unit conductance of approximately 80-120 pS. The polypeptide monomers are capable of transporting potassium ions, have increased potassium ion transporting activity above an intracellular pH of 7.1, and are encoded by nucleic acids that specifically bind to nucleic acids encoding amino acid sequences of the disclosed SEQ ID NOs. Applicants submit that as well as characterizing the functional characteristics of the claimed nucleic acids, they have disclosed a "substantial' use for them in the specification.

On page 2 of the specification, lines 22-35, Applicants explain that cellular signaling in spermatic cells is tightly regulated to prevent inappropriate activation of the irreversible steps that prepare the sperm to fertilize the oocyte. As evidenced by Exhibits A and B, it is known in the art that these essential steps of fertilization are triggered and coordinated by changes in membrane potential, intracellular calcium concentration, and pH level. Between mating and fertilization, sperm undergo capacitation, a process which enables them to penetrate and fertilize an egg. The polypeptide monomers of this invention form potassium channels that open and close depending upon the changes in intracellular pH and membrane potential in spermatocytes. Persons of skill in the art would expect that this opening and closing of the channel is necessary for maintaining the conditions essential for capacitation. Without proper capacitation, fertilization cannot occur.

On page 3, line 15 of the specification, Applicants disclose that the polypeptide monomers of their invention form potassium channels that are regulated by pH levels and are abundantly expressed in spermatocytes. Figures 2A-D demonstrate that expression of the mouse Slo3 transcripts is largely restricted to the testis. On page 12 of the specification, lines 21-34, it is disclosed that spermatocytes that lack Slo3 expression may lack the capability of undergoing capacitation or acrosome reactions. Finally, on page 48 of the specification, lines 30-33, Applicants disclose that modulators of the Slo3 channel may be used to treat infertility conditions due to Slo3's involvement in capacitation and the acrosome reaction.

In the present Office Action, the Examiner alleges that there are no disclosed disease states directed related to Slo3 dysfunction. Applicants respectfully traverse. Infertility is a condition that negatively affects millions of men and women in this country. An extraordinary amount of money and resources is used to treat infertile couples and to fund fertility research. Applicants have shown that persons of skill would believe that Slo3 plays a role in fertilization. This application, therefore, has disclosed a credible, specific, and substantial utility for the claimed polypeptide monomers.

The declaration by Dr. Jegla, in particular, is evidence that the polypeptide monomers of this invention have a substantial utility. As mentioned above, the polypeptide monomers of the present invention form a Slo3 protein channel that is predominantly expressed in spermatocytes and that is regulated by pH levels and changes in membrane potential therein. The application was filed because those of skill in the art believe that Slo3 channels are excellent targets for modulation of sperm function and thereby have a substantial utility.

Dr. Jegla, however, is not the only scientist that believes that potassium channels expressed predominantly in spermatocytes play an important role in fertility. Slo3 channels were discovered by scientists at ICAgen, Inc. ICAgen, Inc. is a privately held company engaged in pharmaceutical discovery and development, focusing exclusively on ion channels as drug targets. ICAgen scientists and investors alike recognize that compounds that increase or decrease the flow of ions by selectively opening or blocking specific channels can aid in the treatment of many diseases. ICAgen, Inc. was formed based on the belief that ion channels play crucial roles in all functions and pathophysiological processes in the human body. Therefore, the scientists at ICAgen understand the importance and utility of polypeptide monomers that form newly discovered potassium channels. Scientists at ICAgen, Inc. believe that the newly discovered and characterized Slo potassium channel is particularly important because it is expressed in spermatocytes and is pH sensitive.

Fertility is a multi-million dollar industry. The cloning of a potassium channel that regulates the process of sperm capacitation has extraordinary implications for fertility treatment. Slo3 channel openers and blockers can be manipulated to either treat infertility or to prevent fertilization depending upon the needs of a patient. A "substantial utility" defines a "real world" use. Clearly, treating fertility is a real world use thereby indicating that the nucleic acids of this invention have a substantial as well as a specific utility.

Finally, the utility of the claimed nucleic acids is credible. Based on the totality of the evidence, one of skill in the art would believe that the channels formed by

the polypeptide monomers play a role in sperm capacitation. Therefore, the polypeptide monomers of the present invention are specific, substantial and credible and thus fulfill the requirements of 35 U.S.C. §101.

D. The nucleic acids of the invention have a well established utility

Assuming *arguendo*, that Applicants neglected to assert a specific, substantial and credible utility in the application, the Examiner should find that, after reading this application, one of skill in the art would immediately appreciate why the invention is useful based on the characteristics of the invention. As explained in the attached declaration, it is well-known that intracellular pH has a profound effect on the viability of mammalian sperm and that alkaline pH is necessary for sperm capacitation and the acrosome reaction. Furthermore, sperm capacitation is known to be accompanied by increases in potassium permeability that hyperpolarize the membrane. This membrane potential is thought to be critical for increasing the driving force for calcium entry, a critical step in the capacitation process. Anyone of skill in the art would recognize that because Slo3 is highly expressed in sperm and is activated by alkalinization, it is an excellent target for the modulation of sperm function. One of skill in the art would realize that by modulating sperm function, it is possible to affect the capacitation process in sperm and to thereby treat fertility. Therefore, it is well-established that a pH sensitive channel expressed predominantly in spermatocytes would be immediately appreciated by one of skill the art. The Examiner should find that the polypeptide monomers of the present invention have a well-established utility.

With these remarks, the Applicants have demonstrated that their invention has a specific, substantial, credible and well-established utility. The Examiner should not find otherwise. Accordingly, this application meets the requirements of 35 U.S.C. § 101.

USPQ 546 (Bd. Pat. App. & Int. 1985); *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). As described in *Wands*, a "considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which experimentation should precede." *Wands*, 8 USPQ2d at 1404 (quoting *In re Jackson*, 217 USPQ 804 (Bd. Pat. App. & Int. 1982).

The pending claims specify stringent hybridization conditions and recite functional elements that allow for the routine identification of the polypeptide monomers of the invention, using the assays provided in the specification. Hybridization methods for the identification of nucleic acids are well known to those of skill in molecular biology. In addition, the claimed functional characteristics of the proteins of the present invention would allow one of skill in the art to identify operable embodiments and exclude inoperable ones. Therefore, Applicants clearly meet the PTO guidelines for enablement, which set forth the standard scope of enablement when a large number of possible embodiments exists. Thus, undue experimentation is not required to practice the claimed invention.

B. The claimed reference sequences provide a meaningful structural feature that allows one of skill to identify the claimed sequences without undue experimentation

The rejection alleges that the specification does not disclose the special technical feature of the invention that is required for activity and the claims do not disclose the precise conditions in which the protein will function as a potassium channel commensurate in scope with the Slo3 channel disclosed in SEQ ID NO:16. However, the claims as amended recite both functional characteristics of the Slo3 potassium channel polypeptide monomers and stringent conditions for hybridization of nucleic acids encoding the polypeptides. The assays and examples of the specification, together with standard methodology known to those of skill in the art, therefore provide adequate guidance for identifying polypeptides polymers of the Slo3 potassium channel.

The assertion of undue experimentation appears to be based on an assumption that enablement requires the description of each and every nucleic acid that could be covered in the invention. As noted below, such a requirement is not consistent with the patent laws. Indeed, it is well settled in the biotechnology art that routine screening of even large numbers of samples is not undue experimentation when a probability of success exists. *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). Using the conditions set forth in the claims and specification and routine methodology, any competent laboratory technician in a molecular biology laboratory could isolate and prepare appropriate constructs, transform cells, and identify those nucleic acids that encode the Slo3 potassium channel polypeptide monomers of the invention. As set forth in MPEP § 2164.08, a rejection for undue breadth is inappropriate where "one of skill could readily determine any one of the claimed embodiments." In the present case, one of skill, given the functional characteristics and the specified hybridization conditions, could easily screen for other polypeptide monomers that fall within the scope of the claims. Therefore, Applicants assert that the provided structural and functional characteristics set forth in the claims and specification enable the polypeptide monomers of the present invention.

The present invention describes polypeptide monomers forming Slo3 potassium channels. Furthermore, the polypeptide monomers have a unit conductance of 80-120 pS, have increased activity above an intracellular pH of 7.1, and hybridize under stringent conditions to reference nucleic acids.

At the time of the present invention, identification of polypeptide monomers having the functional and structural characteristics described above was well within the means of one of skill of the art, without undue experimentation. The present specification provides working examples and discloses standard techniques known to those of skill in the art, for the identification of functional Slo3 polypeptide monomers encoded by nucleic acids that hybridize under specified stringent conditions to nucleic acids encoding an amino acid sequence of SEQ ID NOs:1, 3, 16 or 18. For example, one of skill in the art could use standard hybridization and PCR assays to identify polypeptide

monomers of the invention (*see, e.g.*, specification, pages 23-24 and 27-32). Identification tools, such as nucleic acid screening, hybridization, and PCR techniques, are described in the specification and well known in the art.

Finally, functional assays to identify the pH sensitive voltage-gated potassium channel polypeptide monomers of the invention are known to those of skill in the art and disclosed in the specification. For example, the specification describes methods of expressing a polypeptide monomer of the invention in heterologous cells such as *Xenopus* oocytes or CHO cells, where it forms a pH sensitive potassium channel with voltage gated activity. Methods of measuring pH sensitivity and voltage gated activity are described in the specification on page 14, line 26 to page 15, line 19 and Figures 3-4.

The assays described in the specification, coupled with methodology well known to those of skill in the art, therefore demonstrate that screening for polypeptide monomers having the functional characteristics described above is routine. *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). Applicants therefore respectfully request that the rejection be withdrawn.

C. One of skill in the art could readily determine any one of the claimed nucleic acids

Finally, regarding the issue of enablement for nucleic acids, where a large number of possible embodiments exist, the PTO has provided express guidelines for examination. As set forth in the MPEP § 2164.08, a rejection of such claims such as those in the present application for undue breadth is inappropriate where one of skill could readily determine any one of the claimed embodiments.

In the present Application, one of skill in the art has only to identify polypeptide monomers that (1) hybridize under specified conditions to conserved reference nucleotide sequences of SEQ ID NO:2, 4, 17 or 19; (2) form a potassium channel having a unit conductance of 80-120 pS when expressed in *Xenopus* oocytes; and (3) have increased activity above approximately intracellular pH of 7.1. Routine assays that can be used to identify those channels that have a unit conductance of 80-120

pS when expressed in *Xenopus* oocytes and have increased activity above an intracellular pH of 7.1 are described in the specification and are well known in the art. Nucleic acid screening, hybridization, and PCR techniques are described in the specification and well known in the art. Therefore, although many such polypeptide monomers are possible, one of skill can readily determine, one by one, any polypeptide monomer that forms a pH sensitive potassium channel with the necessary characteristics. Thus, in the present application, the skilled artisan can readily, with only routine experimentation, make and test any particular potassium channel polypeptide monomers.

Rejection under 35 U.S.C. § 112, first paragraph, written description

Claims 17, 19, 21, and 45-56 were rejected as allegedly containing subject matter that was not described in the specification as originally filed. In the Office Action, the Examiner states that that subject matter was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

Applicants respectfully traverse this rejection. The claims fully comply with the requirements for written description of a chemical genus as set forth in *University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997). As described by the Federal Circuit in *Lilly*, "[a] description of a genus of cDNAs may be achieved by means of . . . a recitation of structural features common to the members of the genus . . . ." *Lilly*, 43 USPQ2d at 1406. Furthermore, the court in *Fiers v. Revel* stated that an adequate written description "requires a precise definition, such as by structure, formula, chemical name, or physical properties." *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). The claims set forth both functional elements as well as structural elements, i.e., hybridization conditions. Therefore, the claimed sequences are thereby defined via shared physical and structural properties.

As described above, the present invention relates to the discovery of polypeptide monomers of a new Slo3 pH sensitive potassium channel. The polypeptide monomers are claimed by reference to shared structural features, i.e., nucleic acid

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,

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[(iii)](ii) encoded by a nucleic acid that specifically binds under stringent hybridization conditions to [a nucleic acid sequence of] the nucleic acid disclosed in SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:17 or SEQ ID NO:19, wherein the hybridization reaction is incubated at 37°C in a buffer comprising 40% formamide, 1M NaCl, and 1% SDS, and washed at 45°C in a buffer comprising 1x SSC.

APPENDIX B

PENDING CLAIMS SUBJECT TO EXAMINATION

47. (once amended) An isolated polypeptide monomer of a pH sensitive potassium channel, the monomer:

(i) forming a potassium channel having a unit conductance of 80-120 pS and having increased potassium channel current activity above approximately intracellular pH of 7.1, when the monomer is expressed in *Xenopus* oocyte; and

(ii) encoded by a nucleic acid that specifically binds under stringent hybridization conditions to the complement of a nucleic acid encoding an amino acid sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:16 or SEQ ID NO:18, wherein the hybridization reaction is incubated at 42°C in a buffer comprising 50% formamide, 5x SSC, and 1% SDS, and washed at 65°C in a buffer comprising 0.2x SSC and 0.1% SDS.

48. An isolated monomer of claim 47, wherein the monomer has an amino acid sequence of human or mouse Slo3.

49. An isolated monomer of claim 47, wherein the monomer has an amino acid sequence of SEQ ID NO:1, SEQ ID NO:16 or SEQ ID NO:18.

50. An isolated monomer of claim 47, wherein the monomer has a calculated molecular weight of about 126 kDa.

51. An isolated monomer of claim 47, wherein the monomer is a subunit of a homomeric potassium channel.

52. (once amended) An isolated polypeptide monomer of a pH sensitive potassium channel, the monomer:

(i) forming a potassium channel having a unit conductance of 80-120 pS and having increased potassium channel current activity above approximately intracellular pH of 7.1, when the monomer is expressed in *Xenopus* oocyte; and

(ii) encoded by a nucleic acid that specifically binds under stringent hybridization conditions to the nucleic acid disclosed in SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:17 or SEQ ID NO:19, wherein the hybridization reaction is incubated at 37°C in a buffer comprising 40% formamide, 1M NaCl, and 1% SDS, and washed at 45°C in a buffer comprising 1x SSC.

53. An isolated monomer of claim 52, wherein the monomer has an amino acid sequence of human or mouse Slo3.

54. An isolated monomer of claim 52, wherein the monomer has an amino acid sequence of SEQ ID NO:1, SEQ ID NO:16 or SEQ ID NO:18.

55. An isolated monomer of claim 52, wherein the monomer has a calculated molecular weight of about 126 kDa.

56. An isolated monomer of claim 52, wherein the monomer is a subunit of a homomeric potassium channel.